*Examiner Interview*

Applicants thank the Examiner and her Supervisor for their time during a telephonic interview on July 2, 2002. As requested by the Examiner and her Supervisor, Applicants have refocused their arguments and respectfully request reconsideration.

***Patentability of Claims 1-28 and 62-63 over Stoughton, Chapman, and Barnhill under § 103***

The Action rejects claims 1-28 under 35 U.S.C. § 103(a) as unpatentable over Stoughton, Chapman, and Barnhill. Applicants respectfully disagree that the references render the claimed subject matter obvious. To establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all the claim limitations. (MPEP § 2142.) Each of the claims has at least one limitation not taught or suggested by the references.

***Patentability of Claim 1 over Stoughton***

Claim 1 is directed to a method for quantifying gene relatedness for a plurality of candidate genes and recites:

> for a plurality of selected permutations of the plurality of candidate genes, performing (a)-(c):
>
> (a) . . . constructing a nonlinear model predicting gene expression for the permutation of the plurality of candidate genes;
>
> (b) . . . ;
>
> (c) measuring effectiveness . . . the effectiveness being a quantification of gene relatedness . . . ; and
>
> presenting a plurality of the quantifications of gene relatedness showing relative relatedness for a plurality of the permutations of the genes.

For example, FIG. 11 of the Application shows a possible implementation of the recited technology. FIG. 11 illustrates that a plurality of the quantifications of gene relatedness are presented (e.g., relatedness for $G_3$, $G_4$, and $G_6$; $G_3$, $G_4$, and $G_{10}$, and so on).

*Stoughton's description of "goodness of fit" would not lead one to the recited "presenting a plurality of the quantifications . . . showing relative relatedness for a plurality of the permutations of the genes."* Stoughton describes an example of its technology at column 58, lines 51 et seq.:

> For each pair of experimental comparisons, the data collected consisted of the pairs of the expression levels for each of the 6249 genes. From this genome wide expression data, a subset of 140 expressed genes were selected which

> exceeded the threshold of having changes greater than a factor of two in at least two of the 12 experiments. The two abundance measurements for each of these 140 selected genes in each experiment were used to generate the measure of change, x, according to Section 5.2. The over-all goodness of fit was computed, also according to Section 5.2, which involved normalizing the unnormalized influence matrix of FIG. 7B and finding the best fitting output class from among the seven output classes for each of the 140 selected genes. The goodness of fit of the network model of FIG. 7A (the sum of the individual goodness of fit values for the 140 selected genes) to the yeast expression data was found to be 360.

Thus, Stoughton does describe "a subset of 140 expressed genes were selected." However, selecting *a* subset (i.e., even if a "subset" were to suggest a "permutation") would not lead one of skill in the art to the recited "for a *plurality of selected permutations of . . . genes . . .* constructing a nonlinear model predicting gene expression" as recited by claim 1.

Further, even if Stoughton could somehow be read as suggesting constructing a model for a plurality of selected permutations, it cannot be read to teach or suggest *presenting* relative relatedness *for a plurality of the permutations of the genes.* Stoughton does not teach or suggest presenting any measure (e.g., relative relatedness or goodness of fit) "for a plurality of the permutations of the genes" as recited by claim 1.

*Stoughton's search for better models also would not lead one to the recited "for a plurality of the permutations of the genes."* At column 3, lines 4 et seq., Stoughton states that its object is to provide "methods and systems for the quantitative testing and confirmation of network models of biological pathways." For example, Stoughton describes iteratively refining an initial network hypothesis at column 10, lines 45-52:

> If the new P-value is better than the initial P-value, the refined hypothesis can be used as the base for further refinements in a search for models with even better P-values. The goal of such refinement is convergence of the network models towards one with a P-value below some threshold of significance or towards one that is a useful representation of aspects of the biological system, or the biological subsystem, under study.

Thus, Stoughton does describe searching for models with better P-values. However, mere mention of searching for models would not lead one to the recited arrangement of constructing models and measuring effectiveness *for a plurality of the permutations of the genes*, let alone presenting a plurality of quantifications showing relative relatedness.

As understood by Applicants, Chapman and Barnhill fail to contribute any additional disclosure that would render the claimed arrangement obvious. For at least these reasons, claim 1 and its dependent claims, 2-28 and 62-63, are allowable over the cited art.

***Patentability of Claims 20-26 over Stoughton, Chapman, and Barnhill***

*Stoughton's description of a "network" would not lead one of skill in the art to the recited "neural network."* Claim 20 recites "wherein the nonlinear model predicting gene expression is a neural network predicting gene expression." The rejection of claims 20-26 relies on Stoughton at column 19, lines 35-40, which describes a "network model" and a "network diagram" as follows:

> Using any convenient one of the equivalent representations of the network model, which are, inter alia, as a network diagram, as logical relations, or as a truth table, the predicted responses of each of the classes to each experiment is mechanically determined. These responses are either changes (from "0" to "1" or from "1" to "0") or no changes (from"0" to "0" or from "1" to "1") between two experimental states.

Although Stoughton does describe a "network model," it lists a network diagram, logical relations, and a truth table. None of these teach or suggest using a neural network as recited. Also, as understood by Applicants, Stoughton's drawings show various operators (e.g., "^" on FIG. 4B and FIG.5B), but fail to show a neural network. The rejection thus relies on Chapman on Barnhill for the neural network language.

*Chapman's neural network for predicting the bioactive shape of a molecule would not lead one to a neural network predicting gene expression.* Chapman describes at column 4, lines 61 et seq.:

> A novel modeling approach is proposed using a surface-based representation of molecular shape that employs neural network learning techniques to derive robust predictive models. Trained models predict the bioactive shape of molecules and can be readily interpreted to guide the design of new active compounds.

Thus, although Chapman does describe "neural network learning techniques," the reference describes "predict the bioactive shape of molecules" not "predicting gene expression" as recited in claim 20.

*Barnhill's use of neural network to diagnose disease would not lead one to a neural network predicting gene expression.* Barnhill describes a neural network at column 8, lines 25-29:

> This system provides the capability to screen numerous patient samples for diagnosis and prognosis of disease and enables health care providers to access sophisticated computer-based neural networks specifically trained to diagnose disease with high levels of precision and accuracy.

Thus, Barnhill does describe a neural network is trained to diagnose disease. However, one of ordinary skill in the art could not be expected to surmise the claimed arrangement, which includes "a neural network predicting gene expression," from the description in Barnhill.

*Even if the references did disclose predicting gene expression with a neural network, they would not lead one of skill in the art to the recited arrangement, in which neural networks are constructed "for a plurality of selected permutations . . . of genes."* Even if Chapman or Barnhill could somehow be read as predicting gene expression via a neural network, such a description, without more, would not be sufficient for an obviousness rejection of claim 20. The claim does not merely recite a neural network predicting gene expression, but includes other language distinguishing it over the cited art. Finally, the references lack any motivation to incorporate neural network technology into Stoughton. As understood by Applicants, the stated motivation "to create a more accurate and more understandable model" does not originate from within the references.

For at least these additional reasons, claims 20-26 are allowable over Stoughton, Chapman, and Barnhill.

Various of the dependent claims 21-26 recite additional language not taught or suggested by Stoughton. For example, claim 22 recites a "ternary perceptron." For at least these additional reasons, the dependent claims are separately patentable.

***Patentability of Claims 29-30 under § 103***

Claim 29 is directed to a method for identifying genes related to a target gene and recites:

> ranking the groups of genes other than the target gene by coefficient of determination to present the genes other than the target gene in order of likelihood of relatedness to the target gene.

As understood by Applicants, Stoughton fails to teach or suggest such an arrangement. Applicants fail to find within Stoughton a description of ranking groups of genes, let alone ranking in order of likelihood of relatedness to a target gene. The other references fail to provide sufficient additional disclosure to render the claimed combination obvious.

For these reasons, claim 29 and its dependent claim, 30, are allowable over Stoughton.

***Patentability of Claims 33-35 over Stoughton,Chapman, and Barnhill under § 103***

Claim 33 is directed to a method for identifying related genes and recites:

> training an artificial intelligence function to predict gene expression for the predicted gene.

As understood by Applicants, Stoughton, Chapman, and Barnhill fail to teach or suggest such an arrangement. Similar to the discussion of neural networks above, the references, alone, or in combination fail to describe an "artificial intelligence function to predict gene expression for the predicted gene."

For these reasons, claim 33 and its dependent claims, 34-35, are allowable over the cited art.

***Patentability of the Remaining Claims***

Without belaboring the language of each of the remaining claims, Applicants point out that they recite additional, patentably-distinct subject matter not taught or suggested by a Stoughton-Barnhill-Chapman combination.

***Interview Summary***

The Examiner Interview Summary Record states that "applicant is claiming presenting all related genes." Although all related genes could be presented, as described above, the claims are not so limited. For example, claim 1 is directed to presenting relatedness for "a plurality of the permutations of the genes."

***Request For Interview***

The Examiner is formally requested to contact the undersigned attorney prior to issuance of the next Office Action in order to arrange a telephonic interview. It is believed that a brief discussion of the merits of the present application may expedite prosecution. Applicants submit the foregoing formal Amendment so that the Examiner may fully evaluate Applicants' position, thereby enabling the interview to be more focused.

This request is being submitted under MPEP § 713.01, which indicates that an interview may be arranged in advance by a written request.

***Conclusion***

The claims in their present form should now be allowable. Such action is respectfully requested.

Respectfully submitted,

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